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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,045	01/19/2005	Masashi Okamoto	10873.1576USWO	4002

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EXAMINER	
SHAW, AMANDA MARIE	
ART UNIT	**PAPER NUMBER**
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,045	OKAMOTO ET AL.	
	Examiner	Art Unit	
	Amanda M. Shaw	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *15 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 14-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/4/05 and 12/14/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-25 are currently pending. Applicant's election with traverse of Group I (Claims 1-12) in the reply filed on February 15, 2007 is acknowledged. The traversal is on the grounds that since Group III depends on the method of Group I these claims should also be examined. This argument has been found persuasive therefore the examiner will also examine Group III (Claims 14-25). The applicants further traverse the finding that there is no common special technical feature for the various groups. However it is noted that in the instant application, the linking technical feature of a collecting a microorganism using a water absorbing resin does not constitute a contribution over the prior art. For example, Wardlaw et al (US 2001/0033808) teach a water absorbing resin (i.e. hydrogel) that is used to collect cells or microorganisms from a liquid sample (Abstract). Thus, there is no special technical feature linking the recited groups, as would be necessary to fulfill the requirement for unity of invention.

Therefore claim 13 has been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected subject matter, there being no allowable generic or linking claim.

Accordingly, Claims 1-12 and 14-25 have been examined herein.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-4, 6, and 14-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2-4 and 6 are indefinite because the claims do not recite any active process steps of the claimed method in a positive, active fashion (see Ex parte Erlich 3USPQZd, 101 1 (BPAI 1986)). Since the claims do not recite any active process steps that relate back to the preamble, it is unclear as to how the recited limitations accomplish the method set forth in the preamble of collecting a microorganism or a cell from a liquid sample.

Claim 6 is indefinite over the recitation of the phrases "the amount of the collecting solution" and "the liquid phase part". There is insufficient antecedent basis for these limitations in the claim.

Claims 14-25 are indefinite over the recitation of the phrases "the resultant mixture" and "the extracted gene". There is insufficient antecedent basis for these limitations in the claim.

Claims 15-25 are indefinite over the recitation of the phrase "the collecting solution". There is insufficient antecedent basis for this limitation in the claim.

Claims 16-25 are indefinite over the recitation of the phrase "the heating temperature". There is insufficient antecedent basis for this limitation in the claim.

Claims 16-25 are further indefinite over the recitation of the phrase "wherein the heating temperature is not lower than 70°C and lower than 100°C". This phrase in considered indefinite because it is unclear if it refers to heating temperatures higher

than 100°C (not lower than 100°C) or if it refers to heating temperatures between 70°C and 100°C.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 5, 7, and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Wardlaw (US 2001/0033808 Pub 10/2001).

Regarding Claim 1 Wardlaw teaches a method where formed constituents in an aqueous based fluid sample are separated from the aqueous constituent of the sample so they can be further analyzed. The method comprises placing a liquid sample into a chamber comprised of a hydrophilic hydrogel. The volume of hydrogel in the chamber is sufficient so that the hydrogel will absorb essentially all of the aqueous fraction of the sample. The formed constituents (e.g., cells, bacteria, protozoa etc) may then be harvested from the capture surface of they hydrogel for more detailed examination (Abstract). In the instant case the hydrogel is being interpreted as a water absorbing resin.

Regarding Claim 5, Wardlaw teaches that the volume of the layer of the water absorbent hydrogel is such that when further hydrated, it will absorb essentially all of the

water in the sample (Para 0011). Therefore Wardlaw teaches a method wherein the amount of liquid sample is not greater than the water absorbing capacity of the hydrogel.

Regarding Claim 7 Wardlaw teaches that suitable hydrophilic hydrogel include polyethylene oxide; poly(ethylene oxide-co-propylene oxide); poly(vinyl pyrrolidone); poly(vinyl alcohol); poly(acrylamide); poly(vinyl acetate); poly(acrylic acid) [in Na.sup.+ form]; poly(acrylic acid-co-acrylimide) [in Na.sup.+ form]; poly(acrylic acid) [in Na.sup.+ form]; poly(methacrylic acid) [in Na.sup.+ form]; poly(methacrylic acid-co-acrylamide) [in Na.sup.+ form]; poly(acrylonitrile-co-acrylamide); poly(hydroxyethyl acrylate); poly(hydroxymethyl methacrylate); and hydrophilic poly(urethanes) (Column 0025).

Regarding Claim 10 Wardlaw teaches that examples of fluids that can be analyzed in this fashion include urine; cerebrospinal fluid; pleural fluid; ascites; fluids aspirated from cysts such as thyroid and breast cysts; cytologic specimens which have been placed in an aqueous fluid; platelet-rich plasma; and the like (Abstract).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-4 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wardlaw (US 2001/0033808 Pub 10/2001) in view of Tsuru et al (US Patent 5085781) and in further view of Pathak (US 2002/0114775 Filed 2/2002).

The teachings of Wardlaw are presented above in paragraph 3.

Wardlaw does not teach a method which utilizes a centrifugation tube comprising a filter that divides an inner space of the tube into an upper part and a lower part and hydrogel beads disposed on the filter. Further Wardlaw does not teach a method comprising: pouring a liquid sample into the centrifugation tube and allowing the hydrogel beads in the centrifugation tube to absorb the water wherein the cellular constituents of the sample remain on the surface of the beads; adding a collecting solution to the centrifugation tube to elute the cellular constituents and then centrifuging the collection solution so that the collecting solution and cellular constituents move to the bottom of the tube.

However Tsuru teach a method which utilizes a cylindrical column comprising a filter that divides an inner space of the column into an upper part and a lower part and a separating agent disposed on the filter. Further Tsuru teach a method comprising: pouring a biological fluid into the column and allowing the separating agent in the column to absorb the water wherein the cellular constituents of the sample remain on the surface of the separating agent; adding a collecting solution to was off and recover the cells from the column.

Tsuru does not teach that the separating agent disposed on the filter is a hydrogel bead.

However Pathak et al teach hydrogel beads which can be used for separating biological fluids (Para 0031).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention to have modified the method of Wardlaw and Tsuru by using a centrifugation tube comprising a filter that divides an inner space of the tube into an upper part and a lower part and hydrogel beads disposed on the filter. Using hydrogels to absorb water present in liquid samples was routinely used in the art at the time of the invention as demonstrated by Wardlaw et al. Additionally using filtration combined with centrifugation methods when attempting to recover a given substance by means of elution was routinely used in the art at the time of the invention as demonstrated by Tsuru. Further using hydrogel beads for separating biological fluids was routinely used in the art at the time of the invention as demonstrated by Pathak. Therefore it would have been obvious to one of ordinary skill in the art and well within the skill of the art to combine the teachings of Wardlaw, Tsuru, and Pathak for the benefit of being able to easily collect cells from liquid samples.

5. Claims 8-9 and 14-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wardlaw (US 2001/0033808 Pub 10/2001) in view of Britschgi et al (US Patent 5726021 Issued 10-1998).

The teachings of Wardlaw are presented above in paragraph 3.

Wardlaw et al does not teach that the method is used to collect a microorganism selected from the group consisting of acid-fast bacteria, atypical mycobacteria, gonococcus, legionella bacteria, mycoplasmas, spirochetes, syphilis spirochetes, chlamydiae, rickettsiae, Mycobacterium leprae, Spirillum minus, staphylococci, streptococci, Escherichia coli, Pseudomonas aeruginosa, Pasteurella pestis, viruses, Japanese encephalitis virus, hepatitis B virus, hepatitis C virus, ATLV, HIV, and Ebola virus. Further Wardlaw does not teach a method wherein the acid-fast bacterium is at least one selected from the group consisting of M. avium, M. intracellularae, M. gordonae, M. tuberculosis, M. kansasii, M. fortuitum, M. chelonae, M. bovis, M. scrofulaceum, M. paratuberculosis, M. phlei, M. marinum, M. simiae, M. scrofulaceum, M. szulgai, M. leprae, M. xenopi, M. ulcerans, M. lepraemurium, M. flavescens, M. terrae, M. nonchromogenicum, M. malmoense, M. asiaticum, M. vaccae, M. gastri, M. triviale, M. haemophilum, M. africanum, M. thermoresistable, and M. smegmatis.

However Britschgi et al teach a method of detecting and characterizing different species of Mycobacteria such as M. tuberculosis (Column 6).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Wardlaw et al by collecting M tuberculosis as suggested by Britschgi. There was a strong need for rapid identification of microbial pathogens such as Mycobacterium in the art at the time of the invention as demonstrated by Britschgi et al and thus it would have been obvious to an

ordinary artisan to have collected these microorganisms using the collection method of Wardlaw.

Regarding Claims 14-17, 19, 21-22, and 24-25 Wardlaw et al does not teach a method further comprising extracting a gene of the microorganism or the cell by adding an extraction reagent solution containing a nonionic detergent to the microorganism or the cell and heating the resultant mixture; and amplifying or detecting specifically the extracted gene.

However Britschgi et al teach a method rapid and sensitive detection of Mycobacteria. The method comprises lysing the mycobacterial cells, extracting the nucleic acid from the lysed cells, and amplifying the lysed cells. Specifically Britschgi et al teach that cell lysis is completed by adding to the cell suspension a lysis reagent that contains a nonionic detergent (e.g. triton X which is a polyoxyethyleneglycol p-t-octylphenyl ether), and incubating the suspension at high temperatures. Britschgi et al further teach that the lysis solution typically has a pH between 6.5 and 10.5. The lysis buffer also preferably contains a chelating agent such as EDTA or EGTA. The cells are incubated in the lysis solution between 75°C-99°C until suitable lysis is observed. Typically incubation take 5 minutes or longer at 85°C. Following lysis the nucleic acids are further analyzed via PCR (Columns 8-9).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Wardlaw et al by examining the cellular constituents by performing nucleic acid analysis as suggested by Britschgi. Using nucleic acid analysis as a method to further examine cells collected

from bodily fluids was routinely used in the art at the time of the invention as demonstrated by Britschgi et al and thus it would have been obvious to an ordinary artisan to have examined the collected cells using nucleic acid analysis.

Regarding Claims 18, 20, and 23 the combined references of Wardlaw et al and Britschgi et al do not teach (i) a method wherein the heating is performed at 96.degree. C. for 10 minutes; (ii) a method wherein the concentration of the nonionic detergent in the extraction reagent solution is in a range from 0.01 to 10 wt %; or (iii) a method wherein the concentration of the metal chelating agent in the extraction reagent solution is 0.1 to 100 mM.

However, determining the optimum conditions for performing nucleic acid lysis would have been obvious to one of ordinary skill in the art and well within the skill of the art. As discussed in MPEP 2144.05(b), "(w)here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller,* 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955).

MPEP 2144.05(b):
"Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)"

"A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977)."

6. Claims 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wardlaw (US 2001/0033808 Pub 10/2001).

The teachings of Wardlaw are presented above in paragraph 3.

Regarding Claims 11-12 Wardlaw do not exemplify a method wherein the amount of the liquid sample is in a range from 50 µl to 500 µl or a range from 50 ml to 200 ml.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have adjusted the volume of the hydrogel of Wardlaw based on the amount of liquid in the sample. Using hydrogels to absorb water present in liquid samples was routinely used in the art at the time of the invention as demonstrated by Wardlaw et al and determining the volume of hydrogel to be used when the liquid sample is in a range from 50 µl to 500 µl or a range from 50 ml to 200 ml would have been obvious to one of ordinary skill in the art and well within the skill of the art. Further since Wardlaw teach that the volume of hydrogel in the chamber is sufficient so that the hydrogel will absorb essentially all of the aqueous fraction of the sample, it would be obvious that any amount of liquid sample could be used as long as the appropriate volume of hydrogel was used (Column 0026).

Conclusion

7. No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda M. Shaw whose telephone number is (571) 272-8668. The examiner can normally be reached on Mon-Fri 7:30 TO 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amanda M. Shaw
Examiner
Art Unit 1634

DIANA JOHANNSEN
PRIMARY EXAMINER